IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Kato et al.	
	Art Unit: 1623
Application No.: 10/550,998	Examiner: Henry, Michael C
Filing Date: October 24, 2005	Attorney Ref. No.: TOYA117.005APC
For: THERAPEUTIC AGENT FOR NERVE DAMAGE	

DECLARATION UNDER 37 C.F.R. § 1.132

I, Akiomi Tanaka, declare as follows:

1. I am an employee of Seikagaku Corporation located at 6-1, Marunouchi 1-chome Chiyoda-ku Tokyo 100-0005, Japan, which is engaged in the business of research and development based on glycoscience, among other things.

2. I graduated from the Graduate School of Kitasato University, and was granted Master of Science degree from Kitasato University in March 1998.

3. I have been employed by Seikagaku Corporation since January 2005, and received an appointment to the Central Research Laboratories of Seikagaku Corporation.

4. I am engaged in research in the fields of Orthopedics.

5. I have conducted the experiments described herein and present them as evidence in the above-identified patent application for consideration by the Examiner in support of our Amendment and supporting arguments filed in response to the Office Action mailed on May 4, 2007.

6. The data described herein shows that hyaluronic acid disaccharide to hyaluronic acid 50-saccharide have a superior effect as compared with the hyaluronic acid having larger molecular weight.

7. Methods

Effects of HA4 and HA(900kDa) on spinal cord injury model animal

12-week-old Wister rats (male, purchased from Japan SLC) were used as a model animal, and each body was shaved from the neck to the hip using an electric hair clipper under pentobarbital anesthesia and cleaned with 70% ethanol and Isodine. The dorsal skin was incised to expose thoracic vertebra from T7 to T12, and laminectomy of T9 and T10 thoracic vertebra was performed. Immediately after laminectomy, spinal cord injury was induced by dropping 10g of plumb rod from the height of 25 mm with NYU Impactor. The injured animals were kept warm on a heating mat until they recovered from anesthesia.

After spinal cord injury, a catheter was inserted into subarachnoid cavity between thoracic vertebra T12 and T13, and a single dose of 6 μL (60 μg of HA) of the test substance (HA4 or HA(900kDa)) was administered into marrow cavity with a microsyringe. Six individuals were administered with HA4, and four individuals were administered with HA(900kDa). As a control, six individuals were administered with 6 μl of saline.

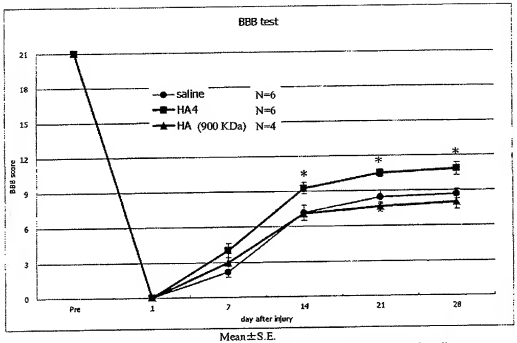
Basso-Beattie-Bresnahan (BBB) test

1, 7, 14, 21, and 28 days after the spinal cord injury, motor function in the hind limb were evaluated in the saline-administered group, HA4-administered group and HA(900kDa)-administered group, respectively, according to the method described by Basso et al.

Statistical analysis

Dunnett's multiple comparison test was preformed between the saline-administered group and the HA-administered groups, and the significant difference was set to be $p < 0.05$ against the physiological saline-administered group.

8. Results



Mean±S.E.
*; p<0.05 by Dunnetts test compared with the saline group.

It was found that HA4 showed a remarkable effect of recovering hind limb-motor function from 14 days after spinal cord injury as compared with the saline-administered group, whereas HA(900kDa) did not recover the hind limb-motor function.

9. I further declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: Akiomi Tanaka
Akiomi Tanaka

Date: August 24, 2007